Summary of Product Characteristics
MONTIGET 10 mg
(Montelukast 10 mg film-coated tablets)

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1. Name of the medicinal product

Montiget Tablets 10 mg

2. Qualitative and quantitative composition

Each film-coated tablet contains montelukast sodium equivalent to 10 mg of montelukast.

Excipient with known effect:
Each film-coated tablet contains 104.60 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

Cream to light-yellow, square-shaped film-coated tablet with a bisect line on one side and plain on the other.

4. Clinical particulars

4.1 Therapeutic indications

Montiget 10 mg is indicated in adults and adolescents 15 years of age and older for:

- the prophylaxis and chronic treatment of asthma, including the prevention of day-time and night-time symptoms, and the treatment of aspirin-sensitive asthmatic patients;
- the relief of symptoms of seasonal allergic rhinitis;
- the prevention of exercise-induced bronchoconstriction.

Lower-strength presentations (chewable tablets and oral granules) are available for younger children.

4.2 Posology and method of administration

Posology

The dose for adults and adolescents 15 years of age and older is one 10 mg tablet daily. For asthma, the dose should be taken in the evening. For seasonal allergic rhinitis, the time of administration may be individualised. Patients with both asthma and seasonal allergic rhinitis should take only one tablet daily in the evening. For the prevention of exercise-induced bronchoconstriction, a single 10 mg dose should be taken at least 2 hours before exercise, and an additional dose should not be taken within 24 hours of a previous dose; patients already taking montelukast daily for another indication should not take an additional dose. The therapeutic effect on asthma-control parameters occurs within one day, and the tablet can be taken with or without food.

Relationship to other asthma therapy

Montelukast can be added to a patient's existing regimen. When a clinical response is evident, the bronchodilator or inhaled-corticosteroid dose may be reduced gradually under medical supervision;

montelukast should not be abruptly substituted for inhaled or oral corticosteroids, and should not be used as monotherapy for exercise-induced asthma.

Paediatric population

The 10 mg tablet is not recommended for children under 15 years; appropriate lower-strength presentations should be used.

Method of administration

For oral use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Montelukast is not indicated for the treatment of acute asthma attacks, including status asthmaticus.

4.4 Special warnings and precautions for use

Montelukast should not be used to treat acute asthma attacks; a suitable rescue short-acting beta-agonist should be available. Montelukast should not be abruptly substituted for inhaled or oral corticosteroids. It does not block bronchoconstriction due to aspirin or other NSAIDs in aspirin-sensitive patients, who should continue to avoid these agents. Patients on montelukast may rarely present with systemic eosinophilia, sometimes with clinical features of vasculitis consistent with Churg-Strauss syndrome; these events have sometimes been associated with a reduction in oral corticosteroid therapy, and physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications and/or neuropathy.

Neuropsychiatric events

Neuropsychiatric events (including agitation, aggressive behaviour or hostility, anxiety, depression, disorientation, disturbance in attention, dream abnormalities, dysphemia (stuttering), hallucinations, insomnia, irritability, memory impairment, obsessive-compulsive symptoms, restlessness, somnambulism, suicidal thoughts and behaviour, tic and tremor) have been reported in adult, adolescent and paediatric patients. Patients and prescribers should be alert for these events; if they occur, the benefits and risks of continuing treatment should be carefully evaluated and discontinuation considered.

Lactose

This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Montelukast had no clinically important effects on the pharmacokinetics of theophylline, prednisone, prednisolone, oral contraceptives, terfenadine, digoxin or warfarin. Phenobarbital reduced the AUC of montelukast by approximately 40%; clinical monitoring is recommended, particularly in children, when potent hepatic enzyme inducers such as phenytoin, phenobarbital or rifampicin are co-administered. Gemfibrozil increased the systemic exposure of montelukast approximately 4.4-fold, though no routine dose adjustment is required. Itraconazole did not significantly increase montelukast exposure.

4.6 Fertility, pregnancy and lactation

Pregnancy

Montelukast should be used during pregnancy only if clearly needed.

Breast-feeding

It is not known whether montelukast is excreted in human milk; caution should be exercised when montelukast is given to a nursing mother.

Fertility

In animal studies, montelukast did not affect fertility or reproductive performance at systemic exposures greatly exceeding the clinical exposure.

4.7 Effects on ability to drive and use machines

Montelukast has no or negligible influence on the ability to drive and use machines. However, individuals have reported drowsiness or dizziness.

4.8 Undesirable effects

The adverse reactions are listed below by System Organ Class and frequency, defined as: common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000) and not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse reaction
Infections and infestations	Common	Upper respiratory tract infection
Blood and lymphatic system disorders	Not known	Increased bleeding tendency
Immune system disorders	Uncommon	Hypersensitivity reactions
	Not known	Anaphylaxis, hepatic eosinophilic infiltration
Psychiatric disorders	Uncommon	Abnormal dreams, nightmares, insomnia, somnambulism, anxiety, agitation including aggressive behaviour or hostility, depression, psychomotor hyperactivity (including irritability, restlessness, tremor)
	Rare	Disturbance in attention, memory impairment, tic
	Not known	Hallucinations, disorientation, suicidal thoughts and behaviour, obsessive-compulsive symptoms, stuttering
Nervous system disorders	Common	Headache
	Uncommon	Dizziness, drowsiness, paraesthesia/hypoaesthesia
	Rare	Seizure
Cardiac disorders	Not known	Palpitations
Respiratory, thoracic and mediastinal disorders	Uncommon	Epistaxis
	Not known	Churg-Strauss syndrome, pulmonary eosinophilia
Gastrointestinal disorders	Common	Abdominal pain
	Uncommon	Diarrhoea, nausea, vomiting, dyspepsia, dry mouth
Hepatobiliary disorders	Uncommon	Elevated ALT and AST
	Not known	Hepatitis (including cholestatic, hepatocellular and mixed liver injury)
Skin and subcutaneous tissue disorders	Uncommon	Rash
	Rare	Bruising, urticaria, pruritus
	Not known	Angioedema, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis
Musculoskeletal and connective tissue disorders	Uncommon	Arthralgia, myalgia including muscle cramps
Renal and urinary disorders	Not known	Enuresis in children
General disorders and administration site conditions	Common	Pyrexia
	Uncommon	Asthenia/fatigue, malaise, oedema

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the National Regulatory Authority.

4.9 Overdose

The most frequently reported symptoms of overdose were consistent with the safety profile and included abdominal pain, somnolence, thirst, headache, vomiting and psychomotor hyperactivity. No specific treatment is available; usual supportive measures should be employed, and it is not known whether montelukast is dialysable.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Leukotriene receptor antagonists. ATC code: R03DC03.

Montelukast is a competitive, selective and orally active leukotriene D4 (cysteinyl leukotriene CysLT1) receptor antagonist. The cysteinyl leukotrienes (LTC4, LTD4 and LTE4) are products of arachidonic acid metabolism released from cells including mast cells and eosinophils; binding of these eicosanoids to CysLT1 receptors is correlated with the pathophysiology of asthma, including airway oedema, smooth-muscle contraction and altered cellular activity. Montelukast inhibits the physiological actions of LTD4 at the CysLT1 receptor without any agonist activity.

5.2 Pharmacokinetic properties

Montelukast is rapidly absorbed, with peak plasma concentrations reached 2 to 4 hours after oral administration and a mean oral bioavailability of 64%. It is more than 99% bound to plasma proteins, with a mean plasma half-life of 2.7 to 5.5 hours in healthy young adults. Montelukast is extensively metabolised in the liver by CYP3A4, CYP2C8 and CYP2C9, and is excreted principally in the faeces via the bile. No dosage adjustment is required in mild to moderate hepatic insufficiency or in renal impairment.

5.3 Preclinical safety data

In animal toxicity studies, minor transient serum biochemical alterations were observed at exposures many-fold higher than the clinical exposure. Montelukast did not affect fertility or reproductive performance, was neither mutagenic nor tumorigenic, and was not phototoxic. It crosses the placenta and is excreted in the breast milk of animals.

6. Pharmaceutical particulars

6.1 List of excipients

- Microcrystalline cellulose
- Lactose monohydrate
- Hydroxypropylcellulose
- Croscarmellose sodium
- Magnesium stearate
- Opadry II Yellow film-coating

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 30°C. Protect from sunlight and moisture. Keep out of the reach and sight of children.

6.5 Nature and contents of container

Alu-Alu blister pack of 14 tablets (2 x 7), presented in a printed carton together with the package insert.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorisation Holder and Manufacturer

Getz Pharma (Private) Limited, 29-30/27 Korangi Industrial Area, Karachi 74900, Pakistan.

8. Marketing Authorisation Number

17771; H2006/334

9. Date of first authorisation / renewal of the authorisation

10. Date of revision of the text